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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/864,169	05/25/2001	Takao Imaeda	208377US0	1449

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/864,169	IMAEDA ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-8 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

Applicants' response to Restriction Requirement, October 2, 2003, filed on October 24, 2003 is acknowledged. Applicant's election with traverse of Group II, claims 9-19 and 14 is acknowledged. Further Applicants have selected thionin as antimicrobial protein A from claim 13, and chaperonin as a partner protein B from claim14. The traversal is on the basis that the office has not established that groups I, II and III are independent and distinct from one another. For example each group is directed to similar subject matter pertaining to fusion proteins. Applicants' arguments have been fully considered but not found persuasive because inventions I and II are related as process of making and product made; inventions I and III are related as product and process of use. As for protein of invention II and nucleic acid of invention III is related to by virtue of the fact that the DNA codes for the protein. Although the DNA and the protein are related, since the DNA encodes the specifically claimed protein, they are distinct inventions because the protein product can be made by other and materially distinct processes, such as purification from the natural source. Further, DNA can be used for processes other than the production of protein, such as nucleic acid hybridization assays. Therefore, the inventions are distinct. Applicants' attention is drawn to the pages 2-3 of the office action of October 2, 2003, where it has been established that groups I, II and III are independent and distinct from one another.

Further Applicants assert that no undue burden would be imposed on the Examiner in conducting an Examination of all three groups together, because similar subject matter is encompassed by each group. In response it should be noted that inventions I, II and III are directed to different subject matter as shown by different classification across the groups. Additionally the issue of the subject matter of each group are different. Therefore, examination of all groups would present a search burden, because the searches of both the patent and non-patent technical literature are not co-extensive. For example a search for DNA does not result in a search of all literature for the protein. In addition a protein and a DNA cannot be substituted one for the other as each has different physical, chemical and biological properties and functions.

The restriction requirement is still deemed proper and is therefore made **FINAL.**

Claims 1-8 and 20 are withdrawn from further consideration by the Examiner as being drawn to a non-elected invention (37 C.F.R 1.142(b)). Therefore, claims 9-19 are currently pending and are under examination.

Objection to the Claims

Claims 13-19 are objected to because the claims describe a sequence that is set forth in the "Sequence Listing " and embedded in the text of the claims and specification. However, no reference is made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the claims. See 37 C.F.R. 1.181(d). This objection may be overcome by providing sequence identifier to the claims.

Claims 16-19 are objected to as to including non-elected species. However, to advance the prosecution, claims will be treated in the light of the Restriction Election. Therefore, only thionin will be examined from claim 13 and chaperonin protein will be examined from claim 14.

Priority

Applicant's claim for foreign priority under 35 U.S.C. 119 (a-d) is acknowledged. This application claims a priority of a Japanese Application No. 2000-161090 filed May 26, 2000. Although the instant application has provided a copy of this application, it fails to provide a certified copy of English translation in support of the priority date claimed. Therefore, the priority date May 25, 2001, would be considered for the priority date, which is a filing date of instant application.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fusion protein comprising a basic antimicrobial protein A, thionin and

a partner protein B, chaperonin; does not reasonably provide enablement for all the fusion proteins composed of any anti microbial protein A and any binding proteins B. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The invention includes a fusion protein comprising a basic antimicrobial protein A having a disulfide bond and a partner protein B having an isoelectric point below pH 7 and a chaperon function (claim 9), wherein the antimicrobial protein A and partner protein B are chemically bonded together (claim 10), wherein the antimicrobial protein A and partner protein B form in series a polypeptide chain through an oligopeptide moiety enzymatically cleavable (claim 11), wherein the antimicrobial protein A and partner protein B form are partially or wholly associated together via hydrophobic affinity or electric properties (claim 12), wherein antimicrobial protein A is a thionin (claim 13) and partner protein B is chaperonin (claim 14), wherein the chaperon function of the partner protein B is a refolding function to modify a wrong bonding position of intramolecular disulfide bond into a right bonding position in the protein A for the active type thereof (claim 15). The specification, however, only discloses cursory conclusions, without data to support the findings. See the discussion below.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the nature of the invention; 2) the breadth of the claims; 3) the predictability or unpredictability of the art; 4) the amount of direction or guidance presented; 5) the presence or absence of working examples; 6) the quantity of experimentation necessary; 7) the state of the prior art; and, 8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The nature of the invention:

The nature of the invention is defined by the claims, which include a fusion protein comprising a basic antimicrobial protein A having a predetermined mode of an intramolecular

disulfide bond, and a partner protein B, having an isoelectric point below pH 7 and a chaperon function. However specification does not provide the information on the specific structure and function of the claimed invention, a predetermined mode of an intramolecular disulfide bond for example. The specification fails to provide a description of the mode of the said intramolecular disulfide bond and how that has been predetermined and what is the function of that mode. The nature of the variation makes it entirely unpredictable what might be considered a variant.

The breadth of the claims:

The breadth of the claims encompasses unspecified number of variants regarding the antimicrobial protein A and a partner protein B, which are not specifically described or demonstrated in the specification. The specification at pages 4 and 9 describes that the invention provides a method for producing antimicrobial protein which comprises expressing as a fusion protein in a prokaryotic cell, a basic antimicrobial protein A having a predetermined mode of an intramolecular disulfide bond as an active type by combining the protein A with a partner protein B having an isoelectric point below pH 7 and a chaperon function; further specification also indicates recovering the fusion protein and modifying and activating the antimicrobial protein A in the fusion protein into the active type by utilizing the function of the partner protein B. However, the specification fails to describe a predetermined mode of an intramolecular disulfide bond in the antimicrobial protein A that is an "active type." The specification also fails to describe the specific chaperon function of the partner protein B. Given the lack of teachings or guidance in applicants' disclosure regarding the fusion protein comprising an antimicrobial protein A and the partner protein B other than the one specifically referenced thionin and PDI, it would require undue experimentation by one skill in the art to make fusion proteins of current invention or other undefined molecules having an activity substantially equivalent to that of the fusion protein exemplified at pages 14-17, commensurate in scope with the claims. The specification indicates the general methods of generating fusion protein claimed. The specification fails to provide the positions in the sequence, which are critical to the protein's structure/function relationship, such as sites or regions directly involved in binding and activity.

The amount of direction or guidance presented;

The presence or absence of working examples; and

The quantity of experimentation necessary:

Given the breadth of the claims in the invention, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to make and use the variants of broadly claimed group of fusion proteins. Such teachings are absent in the specification. The specification has disclosed a fusion protein composed of a antimicrobial protein A having a predetermined mode of an intramolecular disulfide bond, and a partner protein B, wherein the antimicrobial protein selected is thionin (claim 13) and partner protein selected is chaperon (claim 14) for the current prosecution. There is no guidance as to how the functional protein A and B would be generated for the fusion protein of the invention (claim 12 requires a fragment of the protein B. The specification has provided no guidance to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein, which are tolerant to change (e.g. the active site), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active protein variants, this is not adequate guidance as to the nature of active derivatives that may be constructed. The working examples are exclusively drawn to making one fusion protein, wherein the hybrid is composed of thionin and PDI and also thionin and acid protein (see Example 1-4). However, PDI and acid protein are non-elected species. Specification fails to provide a description of a fusion protein composed of thionin (as antimicrobial protein) and chaperon (as a partner protein).

In consideration of each of factors, it is apparent that undue experimentation is necessary because in summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants, the guidance/the teaching in the specification is limited, and the outcome is unpredictable for the various modified forms. It is necessary to have additional guidance to carry out further experimentation to assess the property of the variants. Therefore, due to large quantity of experimentation necessary to generate the infinite number of variants and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required to in order to provide activity, the absence of working examples directed to same, the complex nature of the invention and the breadth of the claims,

which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 9-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 is indefinite as to the phrase "predetermined mode." It is not clear as to the structure of the antimicrobial protein A, which has a predetermined mode of an intramolecular disulfide bond as an active type. Claims 10-15 are included in this rejection for being depend from a rejected base claim and not correcting the deficiency of the claim from which they depend.

Claim 12 is indefinite for using the word "partially." It is not clear what is the size, structure and function of that portion of antimicrobial protein A and/or partner protein B that are associated together via hydrophobic affinity or electric properties.

Claim 15 is rejected as to the word "wrong" and "right" bonding position. It is not clear what is 'wrong" and what is "right" in relation to the structure of protein A.

Conclusion

No claims are allowable.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 10:00 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rita Mitra, Ph.D.
January 11, 2004

ROBERT A. WAX
PRIMARY EXAMINER